REMARKS

Claims 23, 25, 27, 29, 33, 35, 36, 39, 40, 43, 44, 47, 48, 60-67, 73, 74, 77, 78, 81, 82, 85 and 86 are herein amended. Attached hereto is a marked-up version of the changes made by the current amendments, captioned "Version With Markings To Show Changes Made." The amendments are fully supported by the specification and claims as originally filed, and thus no new matter has been added.

In the instant Office Action, the Examiner indicates that claims 21-29, 33-36, 39-40, 43-44, 47-49, 59-67, 72-74, 77-78, 81-82, and 85-86 are pending. However, claim 49 was canceled in the amendment filed May 31, 2001. Accordingly, Applicants believe that claims 21-29, 33-36, 39-40, 43-44, 47-48, 59-67, 72-74, 77-78, 81-82, and 85-86 are currently pending in the instant application. Claims 21, 22, 24, 26, 28, 59, 60, 62, 64 and 66 are allowed by the Examiner, for which the Applicants thank the Examiner.

I. Amendment of the Claims to Correct a Clerical Error

Claims 21-96 were added in the response filed October 17, 2000. As filed, claims 23-96 were erroneously numbered as claims 24-97. In accordance with this clerical error, claims 27, 29, 35, 36, 39, 40, 43, 44, 47, 48, 60-67, 73, 74, 77, 78, 81, 82, 85 and 86 recited the incorrect antecedent claim number.

Thus, claims 27, 29, 35, 36, 39, 40, 43, 44, 47, 48, 60-67, 73, 74, 77, 78, 81, 82, 85 and 86 are herein amended to depend from the correct, properly numbered antecedent claims. Accordingly, no new matter has been added by way of these amendments.

II. Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has maintained the rejection of claims 23, 25, 27, 29, 33, 36, 39, 40, 44, 48, 49, 61, 65, 67, 74, 78, 82 and 86 for allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, the Examiner contends that:

> The claims, as written, embrace any amino acid sequences which are heterologous to SEQ ID NO:2, or portions thereof as indicated. If Applicant intends to claim polypeptides comprising SEQ ID NO:2 and further comprising a heterologous polypeptide fused to the polypeptide of SEQ ID NO:2 and further comprising a heterologous polypeptide fused to the polypeptide of SEQ ID NO:2 . . . then the claims should be amended appropriately.

See page 3 of Paper No. 19.

As a preliminary matter, Applicants point out that claim 49 was canceled in the amendment filed on May 31, 2001.

With regard to claim 39, Applicants disagree and traverse the rejection. The Examiner's arguments are directed exclusively toward claims embracing amino acid sequences heterologous to SEQ ID NO:2 or portions thereof. Claim 39 reads on a polypeptide that is 95% or more identical to amino acids 2 to 381 of SEQ ID NO:2. As such, the arguments put forth by the Examiner are clearly not applicable to claim 39. Accordingly, Applicants request that the Examiner reconsider and withdraw the rejection of claim 39 under 35 U.S.C. § 112, second paragraph.

With regard to claims 23, 25, 27, 29, 33, 36, 40, 44, 48, 61, 65, 67, 74, 78, 82 and 86, Applicants also respectfully disagree for the reasons put forth in the responses dated May 31, 2001 and November 14, 2001. However, claims 23, 25, 27, 29, 33, 36, 40, 44,

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48, 61, 65, 67, 74, 78, 82 and 86 are herein amended to comply with the wording preferred by the Examiner.

In light of the above remarks, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 23, 25, 27, 29, 33, 36, 39, 40, 44, 48, 49, 61, 65, 67, 74, 78, 82 and 86 under 35 U.S.C. § 112, second paragraph.

III. Rejections Under 35 U.S.C. § 112, first paragraph for lack of written description

The Examiner has also maintained the rejection of claims 23, 25, 27, 29, 33-36, 43, 44, 47, 48, 59, 61, 63, 65, 67, 72-74, 77, 78, 81, 82, 85 and 86 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *See* Paper No. 11, page 6. Specifically, the Examiner contends that Applicants' previous statements are unpersuasive and that "the disclosure of the polypeptide sequence and functional activity of SEQ ID NO:2 does not adequately describe a representative number of polypeptides which are varied, such that 95% identity to SEQ ID NO:2 remains and functional activity is maintained." *See* Page 4 of the instant Office Action.

Applicants respectfully disagree and traverse.

Firstly, Applicants note that, as herein amended, claims 23, 25, 27, 29, 33, 59, 61, 63, 65 and 67 do not read on variants of SEQ ID NO:2, as alleged by the Examiner. Indeed, claims 23, 25, 27, 29, and 33 are drawn to SEQ ID NO:2 or a specific portion thereof fused to a heterologous polypeptide. Likewise, claims 61, 63, 65 and 67 read on the polypeptide encoded by the deposited clone or a specific portion thereof fused to a heterologous polypeptide. Claim 59 is a Markush claim directed to polypeptides

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comprising the full-length or specific portions of the polypeptide encoded by the deposited clone. Accordingly, the arguments put forth by the Examiner are not relevant to claims 23, 25, 27, 29, 33, 59, 61, 63, 65 and 67 and Applicants respectfully request that the rejection of these claims be withdrawn.

Furthermore, claims 34 and 72 (and, accordingly, dependent claims 35, 36, 39-44, 47 and 48; and 73, 74, 77, 78, 81, 82, 85 and 86 respectively) are herein amended to embrace specific polypeptides of SEQ ID NO:2 or encoded by the deposited clone that stimulate cellular proliferation. Thus, disclosure in the specification of both the polypeptide sequence and functional activity of that sequence adequately describe the genera encompassed by claims 34-36, 39-44, 47-48, 72-73, 77, 78, 81, 82, 85 and 86.

In light of the above remarks and amendments made herein, the rejection is clearly not relevant to the pending claims. Moreover, Applicants respectfully assert that improper standards were used to support this rejection.

For example, it is asserted that disclosure of a "representative number of species" is required to comply with the written description requirement of 35 U.S.C. § 112 for genus claims. The Examiner claims that support for this assertion is found in the Revised Interim Written Description Guidelines (*see* Paper No. 11, page 6). However, examination of the Written Description Guidelines, as well as the M.P.E.P., reveals that the proper legal test for written description is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. M.P.E.P. § 2163.02. *See also Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991). Both sources further teach that possession may be shown in a variety of ways, including description of an actual reduction to practice (i.e., disclosing a representative number of species) **or** disclosing drawings or

structural chemical formulas that show that the invention was complete **or** by a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Accordingly, satisfaction of the written description requirement is not based exclusively on whether the specification describes a representative number of species. Indeed, such a description is simply one means for showing possession. Applicants assert that the instant application fulfills at least the other means for satisfying the written description requirement.

For example, it is well established that a "gene is a chemical compound, albeit a complex one". *Amgen, Inc. v. Chugai Pharmaceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to, for example, polypeptides having at least 95% identity to SEQ ID NO:2 (or of the polypeptide encoded by the cDNA of the claimed deposit), are essentially chemical claims involving generic chemical formulas. As stated by Judge Lourie in *Regents of the University of California v. Eli Lilly & Co.*, (119 F.3d 1559, 1569, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997)), "In claims involving chemical materials, *generic formulae* usually indicate with specificity what the generic claims encompass. *One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass.*" (Emphasis added).

Indeed, all of the objectives met by a generic chemical formula are similarly met by the explicit description in the instant specification of a both polynucleotide and polypeptide sequence (*i.e.* SEQ ID NOS:1 and 2) and claims to polypeptides that are 95% identical over the full length of the amino acids of that sequence. That is, the instant claims explicitly distinguish the boundaries of each claimed genus and identify all of the members of each genus. For example, the skilled artisan could clearly envision each of

the polypeptides that are 95% identical to the polypeptide of SEQ ID NO:2 as a polypeptide with 1, 2, 3, 4, or 5 amino acid substitutions for each 100 amino acids along its length. Nothing more than a basic knowledge of the genetic code and what is described in the specification would be required for the skilled artisan to readily envision every single one of the claimed polypeptides that are 95% identical to the amino acid sequence of CTGF-2. Undoubtedly, such knowledge is well within what is expected of the skilled artisan. Accordingly, the instant specification satisfies the written description requirement of 35 U.S.C. § 112, first paragraph.

As a final matter, Applicants note that an improper legal standard was used to support the instant rejection. For example, the assertion that "[n]o mutagenesis data has been provided" (*see* page 4), is inconsistent with the law and the examining guidelines. M.P.E.P. § 2138.05 states that:

> [R]eduction to practice may be an actual reduction or a constructive reduction to practice which occurs when a patent application on the claimed invention is filed. The filing of a patent application serves as conception and constructive reduction to practice of the subject matter described in the application. Thus, the inventor need not provide evidence of either conception or actual reduction to practice when relying on the content of the patent application.

(emphasis added; citations omitted). Accordingly, it is not necessary that Applicants have actually generated all the species encompassed within the claimed invention, so long as one of ordinary skill would recognize the claimed invention from the disclosure.

Additionally, the assertion that "[t]he scoped claimed in not enabled by the instant disclosure since no reasonable number of homologues of SEQ ID NO:2 have been disclosed . . ." (page 4) is also not a proper basis for a rejection under written description. As noted in the response filed November 14, 2001, the written description requirement is

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separate and distinct from the enablement requirement. M.P.E.P. § 2161. The proper legal standard for written description is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. M.P.E.P. § 2163.02.

In light of the above amendments and remarks, it is clear that one skilled in the art would reasonably conclude upon reading the present application as filed, that Applicants had possession of the polypeptides encompassed by the rejected claims. Furthermore, no evidence was provided to rebut this assertion.

For all of the above reasons, Applicants respectfully request that the rejection of claims 23, 25, 27, 29, 33-36, 43, 44, 47, 48, 59, 61, 63, 65, 67, 72-74, 77, 78, 81, 82, 85 and 86 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

IV. Rejections Under 35 U.S.C. § 102(b)

The Examiner has further upheld the rejection of claims 23, 25, 27, 29, 33, 36, 40, 44, 48, 61, 63, 65, 67, 74, 78, 82 and 86 under 35 U.S.C. § 102(b) as being anticipated by Purchio et al. In particular, the Examiner contends that Applicants' prior showing that the prior art reference does not anticipate every element of the claims is not persuasive because "[t]he limitation of SEQ ID NO:2 cannot be implied from the language of the claims as they are presently written." *See* page 5.

Applicants respectfully disagree and traverse. However, Applicants point out that claims 23, 25, 27, 29, 33, 36, 40, 44, 48, 61, 63, 65, 67, 74, 82 and 86 are herein amended to read upon SEQ ID NO:2 or specific portions thereof fused to a heterologous polypeptide. For example, claim 23 reads on amino acids 1 to 381 of SEQ ID NO:2 fused

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to a heterologous polypeptide. As such, these claims specifically require the element of SEQ ID NO:2.

To anticipate a claim, the prior art reference must teach, either explicitly or inherently, each and every element of the claim. *See* M.P.E.P. § 2131. As stated in the response filed November 14, 2001, Purchio et al. does not teach, explicitly or inherently, the element SEQ ID NO:2, which is recited in each of the rejected claims. Thus, Purchio cannot anticipate any of the rejected claims. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. Applicants believe that this application is in condition for allowance. If in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below.

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If there are any fees due in connection with the filing of this paper, please charge the fees to Deposit Account No. 08-3425.

Respectfully submitted,

Dated: May 29, 2002

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Li et al. Docket No.: PF126P1D1

Application No.: 09/348,815 Group Art Unit: 1635

Filed: July 8, 1999 Examiner: J. Zara

For: Connective Tissue Growth Factor-2

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Please replace the first paragraph of the specification with the following paragraph.

-- This application is a divisional of U.S. Patent Application Serial No. 08/459,101, filed June 2, 1999, ~~pending~~ now U.S. Patent No. 5,945,300, granted August 31, 1999, which is a continuation-in-part of, and claims priority under 35 U.S.C. § 120 to U.S. Patent Application Serial No. PCT/US94/07736, filed July 12, 1994, both of which are incorporated by reference in their entireties.--

In the claims:

Claims 23, 25, 27, 29, 33-36, 39, 40, 43, 44, 47, 48, 60-67, 72-74, 77, 78, 81, 82, 85 and 86 are amended as follows.

23. (Once Amended) The polypeptide of claim 22, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

25. (Once Amended) The polypeptide of claim 24, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

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27. (Once Amended) The polypeptide of claim 2~~7~~6,wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

29. (Once Amended) The polypeptide of claim 2~~9~~8, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

33. (Once Amended) The polypeptide of claim 22, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

34. (Twice Amended) An isolated polypeptide comprising a first amino acid sequence that is at least 95% identical to a second amino acid sequence selected from the group consisting of:

(a) amino acids 1 to 381 of SEQ ID NO:2;

(b) amino acids 2 to 381 of SEQ ID NO:2;

(c) amino acids 25 to 381 of SEQ ID NO:2; and

(d) a polypeptide fragment of SEQ ID NO:2, ~~wherein said fragment stimulates cellular proliferation.~~

wherein said polypeptide or polypeptide fragment stimulates cellular proliferation.

35. (Once Amended) The polypeptide of claim 3~~5~~4, wherein said second amino acid sequence is (a).

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36. (Once Amended) The polypeptide of claim 3~~6~~5, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

39. (Once Amended) The polypeptide of claim 3~~5~~4, wherein said second amino acid sequence is (b).

40. (Once Amended) The polypeptide of claim 4~~0~~39, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

43. (Once Amended) The polypeptide of claim 3~~5~~4, wherein said second amino acid sequence is (c).

44. (Once Amended) The polypeptide of claim 44~~3~~, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

47. (Once Amended) The polypeptide of claim 3~~5~~4, wherein said second amino acid sequence is (d).

48. (Once Amended) The polypeptide of claim 4~~8~~7, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to SEQ ID NO:2~~.

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60. (Once Amended) The polypeptide of claim ~~60~~59, wherein said amino acid sequence is (a).

61. (Once Amended) The polypeptide of claim 6~~1~~0, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to the polypeptide encoded by the human cDNA contained ATCC Deposit Number 75804~~.

62. (Once Amended) The polypeptide of claim ~~60~~59, wherein said amino acid sequence is (b).

63. (Once Amended) The polypeptide of claim 6~~3~~2, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to the polypeptide encoded by the human cDNA contained ATCC Deposit Number 75804~~.

64. (Once Amended) The polypeptide of claim ~~60~~59, wherein said amino acid sequence is (c).

65. (Once Amended) The polypeptide of claim 6~~5~~4, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to the polypeptide encoded by the human cDNA contained ATCC Deposit Number 75804~~.

66. (Once Amended) The polypeptide of claim ~~60~~59, wherein said amino acid sequence is (d).

67. (Once Amended) The polypeptide of claim 6~~7~~6, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to the polypeptide encoded by the human cDNA contained ATCC Deposit Number 75804~~.

72. (Twice Amended) An isolated polypeptide comprising a first amino acid sequence that is at least 95% identical to a second amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of the full-length polypeptide encoded by the human cDNA contained in ATCC Deposit Number 75904;

(b) the amino acid sequence of the full-length polypeptide, lacking the N-terminal methionine, encoded by the human cDNA contained in ATCC Deposit Number 75904;

(c) the amino acid sequence of the mature polypeptide encoded by the human cDNA contained in ATCC Deposit Number 75904; and

(d) a polypeptide fragment of the polypeptide encoded by the human cDNA contained in ATCC Deposit Number 75904; ~~wherein said fragment stimulates cellular proliferation.~~

wherein said polypeptide or polypeptide fragment stimulates cellular proliferation.

73. (Once Amended) The polypeptide of claim 7~~3~~2, wherein said second amino acid sequence is (a).

74. (Once Amended) The polypeptide of claim 74~~3~~, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to the polypeptide encoded by the human cDNA contained ATCC Deposit Number 75804~~.

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77. (Once Amended) The polypeptide of claim 7~~3~~2, wherein said second amino acid sequence is (b).

78. (Once Amended) The polypeptide of claim 7~~8~~7, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to the polypeptide encoded by the human cDNA contained ATCC Deposit Number 75804~~.

81. (Once Amended) The polypeptide of claim 7~~3~~2, wherein said second amino acid sequence is (c).

82. (Once Amended) The polypeptide of claim 8~~2~~1, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to the polypeptide encoded by the human cDNA contained ATCC Deposit Number 75804~~.

85. (Once Amended) The polypeptide of claim 7~~3~~2, wherein said second amino acid sequence is (d).

86. (Once Amended) The polypeptide of claim 8~~6~~5, wherein the ~~comprising an~~ amino acid sequence is fused to a heterologous polypeptide ~~to the polypeptide encoded by the human cDNA contained ATCC Deposit Number 75804~~.

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